THE HUMAN VARIOME PROJECT

an NGO official partner of UNESCO

Global Globin 2020 Challenge

USM UNIVERSITI SAINS MALAYSIA

APEX™

SETTING UP DIAGNOSTIC NGS APPLICATION IN MALAYSIA

PROF ZILFALIL ALWI, *MBBS, MMed, PhD*

HUMAN GENOME CENTRE, USM MALAYSIA

OUTLINE

- **Next Generation Sequencing (NGS)**
  - Introduction
  - Common use of NGS
- **Genetic services in Malaysia**
  - Genetic diseases in Malaysia
  - Allocation from the Malaysian Government
  - History of genetic diagnostic services In Malaysia
  - Genetic testing in Malaysia
- **Delivering NGS to Malaysia Diagnostic Setting**
- **Building Blocks**
  - Guidelines for diagnostic NGS
  - Requirement for clinical diagnostic application
  - Issues to address
- **Summary**

NEXT GENERATION SEQUENCING

- Uses array-based sequencing that combines techniques developed in Sanger sequencing to process millions of reactions in parallel.

- Result in very high speed & throughput at a reduced cost.

- Developments in NGS DNA sequencing technology:

    - Allow data production to far exceed the original description of Sanger sequencing
    - Enable revolutionary advances in our understanding of health and disease.

Sequencing technology is the engine that powers the car that
allows us to navigate the human genome roadmap.
As that engine becomes ever more powerful, so will the questions we can ask and answer
about the geography of our genetic landscape

Elaine R. Mardis, 2011
NATURE | VOL 470 | 2011

Photo credit: Illumina

COMMON USE OF NGS

- Molecular biology
- Gene expression
- Environmental genomics
- Evolutionary biology & population genetics
- Prenatal screening
- Personalised medicine
- Forensic application

Patients

Genomics
Whole Genome Sequencing
Whole Exome Sequencing

Transcriptomics
RNA-Seq

Epigenomics
Bisulfite-Seq
ChiP-Seq

Technologies

- Point Mutation
- Indels
- Copy Number Variation
- Structural Variation
- Differential Expression
- Gene Fusion
- Alternative Splicing
- RNA Splicing
- Methylation
- Histone Modification
- Transcription Factor Binding

Data Analysis

- Functional effect of mutation
- Network & Pathway Analysis
- Integrative Analysis

Interpretation

Further Understanding of Clinical Applications

JAMES WATSON SEQUENCED

2007

1st whole human genome sequenced with NGS technology for less than $1 million

24.5 billion bases of genomic DNA sequences generated

3.6 million variants detected including disease susceptibility gene associations

James Watson	Human Genome Project
454 Life Sciences, Roche	Sanger
2 months	10-13 years
< $1 million	$100 million - $2.7 billion
7.4 fold coverage	7.5 fold coverage

www.roche-applied-science.com

INDIVIDUALS OF DIFFERENT ETHNICITY SEQUENCED

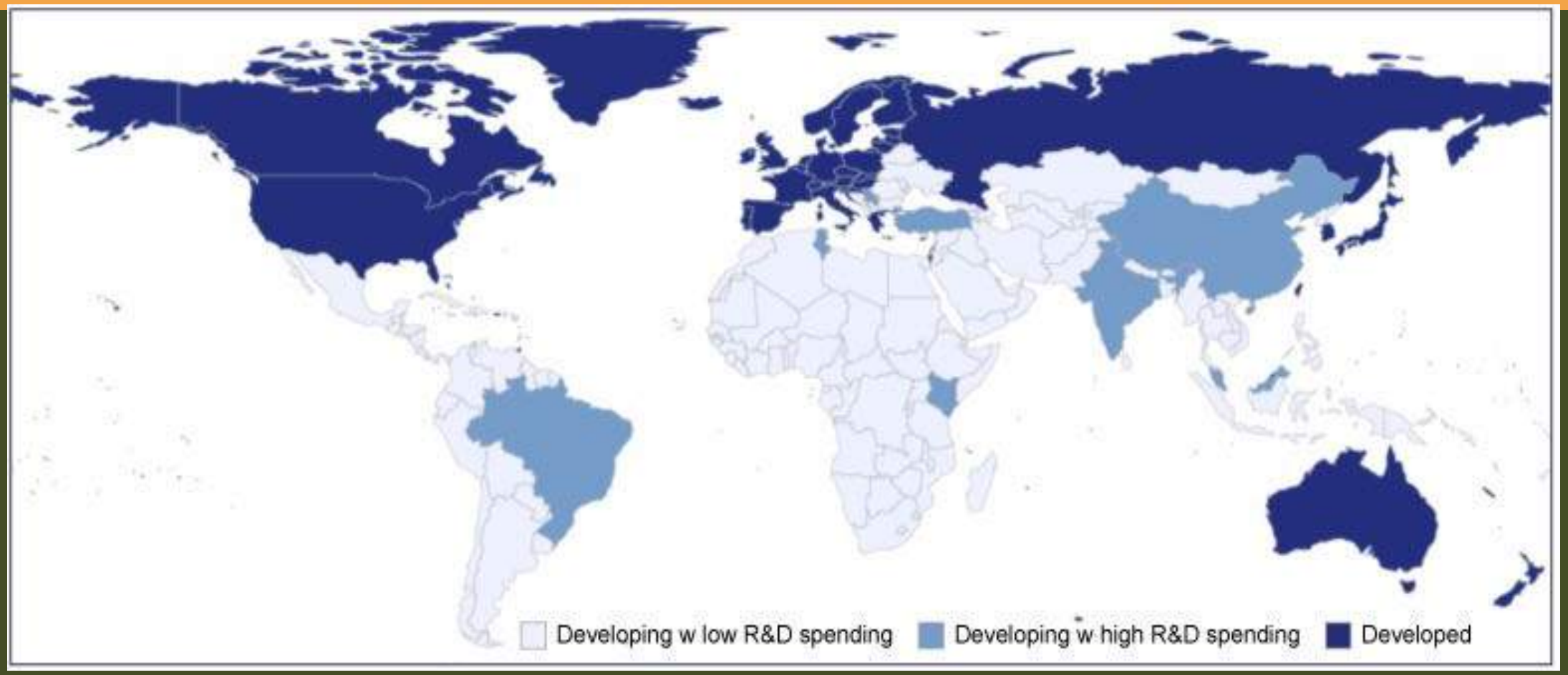
USA	Caucasians (J. Craig Venter) Levy et al 2007 ; (Watson) Wheeler et al 2008
China	Male Han Chinese Wang et al 2008
Nigeria	Male Yoruban Bentley et al 2008
Korea	Korean male Ahn et al 2009
Japan	Japanese male Fujimoto et al 2010
India	South Asian Indian female Gupta et al 2012
Spanish	Spanish family Corpas et al 2013
Singapore	Singapore Malays Wong et al 2013
Malaysia	Malays (male Royal Kelantan Malay) Juhari et al 2014

https://www.dreamstime.com

GENETIC SERVICES IN MALAYSIA

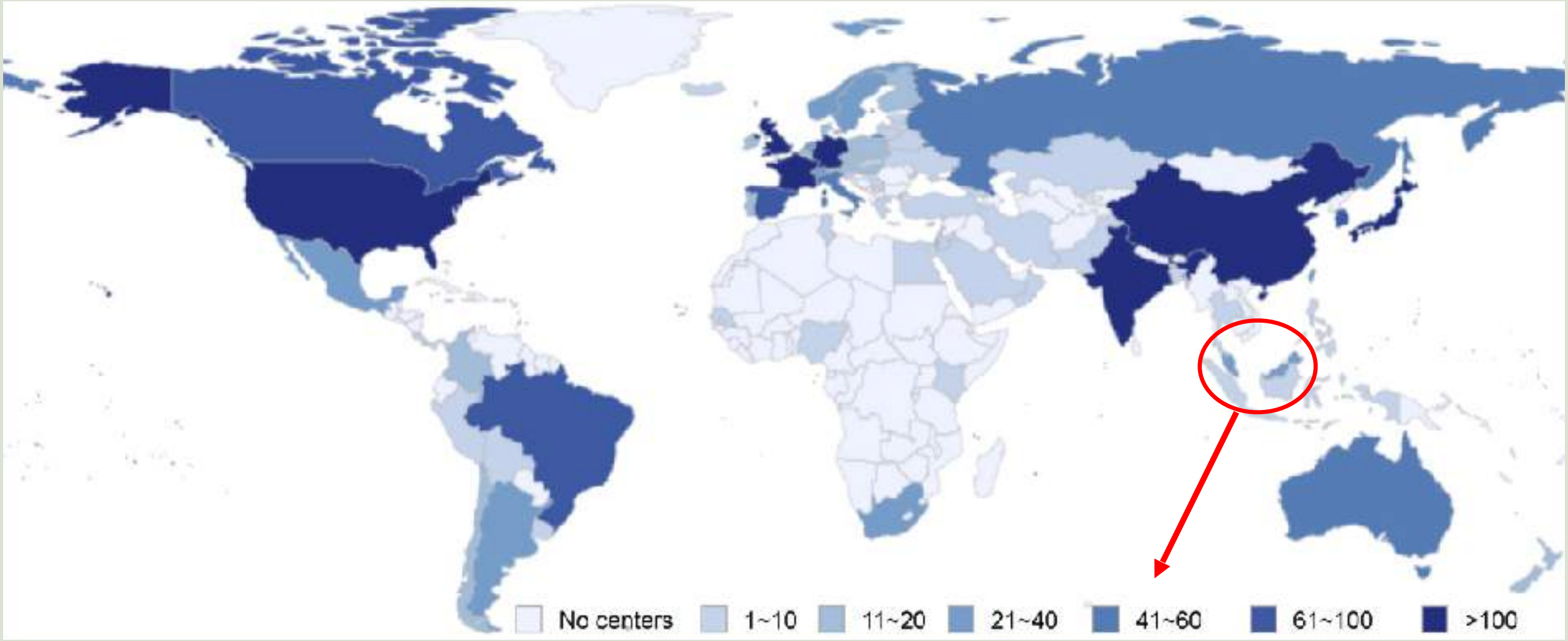
Developing and Developed Countries

(Current state of genome sequencing technologies worldwide)



Ref: Helmy at al 2016

Genome Sequencing Centres In The World



Ref: Helmy at al 2016

GENETIC DISEASES IN MALAYSIA

- 3% or 16,500 of Malaysia's 550,000 babies are afflicted with congenital abnormalities
  - genetic disorders, chromosomal disorders & inherited metabolic diseases

- Common genetic diseases in Malaysia
  - Down syndrome (1:700)
  - Beta Thalassemia Major (1:2000) (0.05%)
  - G6PD (glucose-6-phosphate dehydrogenase) deficiency
  - Duchenne Muscular Dystrophy (DMD)
  - Muscular Atrophy (SMA)
  - Retinoblastoma
  - Orofacial Cleft

Source:
1. Halim Fikri *et al* 2015
2. Prof Dr Thong Meow Keong, December 5, 2016 https://mypositiveparenting.org/2016/12/05/genetic-disorders-affecting-children/

ALLOCATION FROM MALAYSIAN GOVERNMENT (2018)

Ministry of Health

- RM27 billion allocated for health care out of RM280.25 billion 2018 budget **(9.6%)**
  - RM10 million allocated for the treatment of increasing cases of rare diseases.
  - RM30 million for Healthy Community Empowers the Nation programme to create awareness on non-communicable diseases in 10,000 locations nationwide.
- RM30 million to Malaysian Healthcare Travel Council (MHTC) to promote Malaysia as the Asian Hub for Fertility Treatment

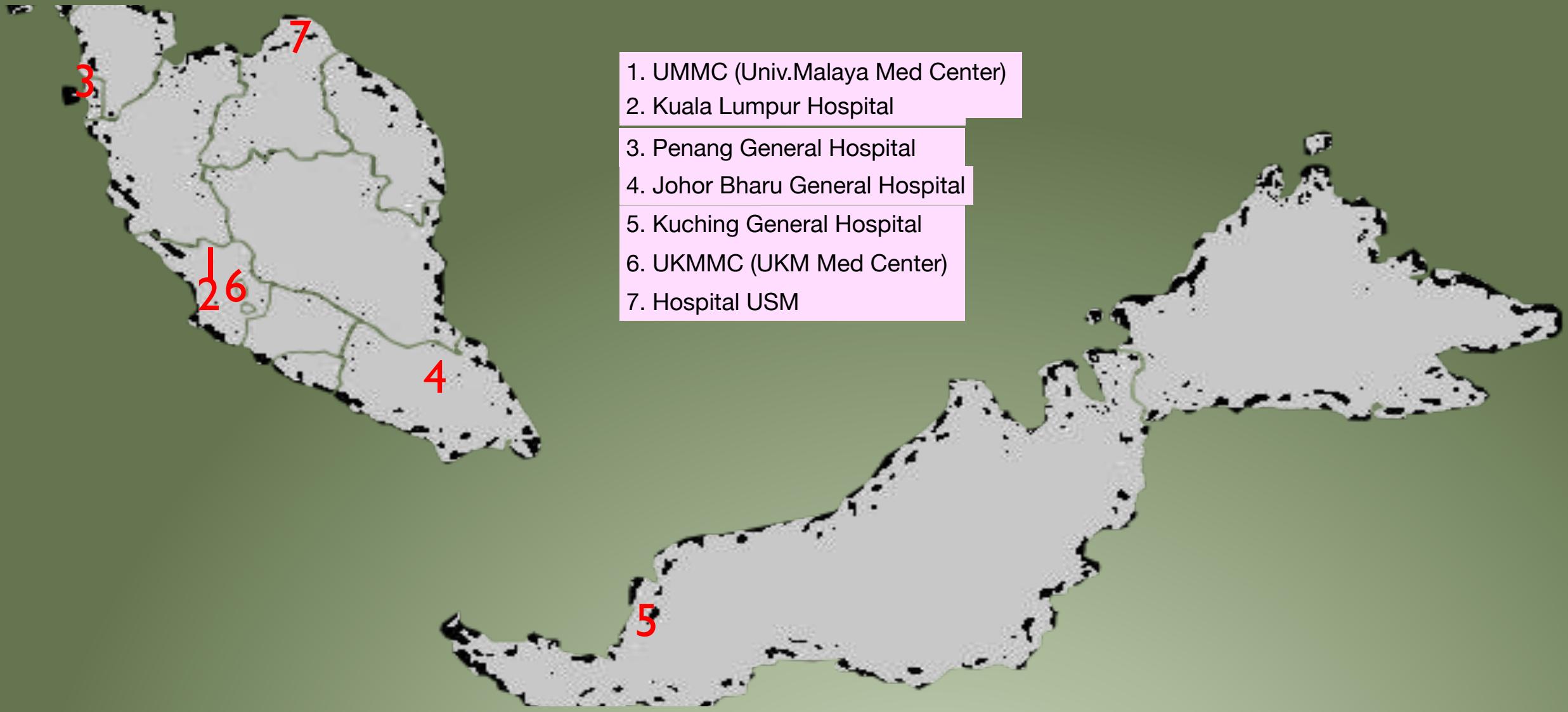
No specific budget for genetics and biotechnology

Ministry of S

- RM30 milli nstitute, Malaysia Institute of Pharmaceuticals & Neutrceuticals) (**2.63%** of total MOSTI budget)
- RM100 million (soft loans) through Bioeconomy Corporation under 11th Malaysia Plan to assist BioNexus SMEs & matured companies in growing & expanding existing bio-based businesses.

Ministry of Education

- RM400 million for R&D grants provided to Public Institute of Higher learning (IHLs)
- Total percentage of R&D to GDP per annum in Malaysia is: **1.1%** (ideally 2%)



1. UMMC (Univ.Malaya Med Center)
2. Kuala Lumpur Hospital
3. Penang General Hospital
4. Johor Bharu General Hospital
5. Kuching General Hospital
6. UKMMC (UKM Med Center)
7. Hospital USM

GENETIC DIAGNOSTIC CENTERS IN MALAYSIA

BIOTECHNOLOGY & GENOMIC RESEARCH INSTITUTES

MINISTRY OF SCIENCE, TECHNOLOGY & INNOVATION MALAYSIA

- Malaysia Genome Institute (MGI)
- Malaysia Agro-Biotechnology Institute (ABI)
- Malaysian Institute of Pharmaceuticals & Nutraceuticals

Kuala Lumpur & Selangor

Government Institutions including government funded universities

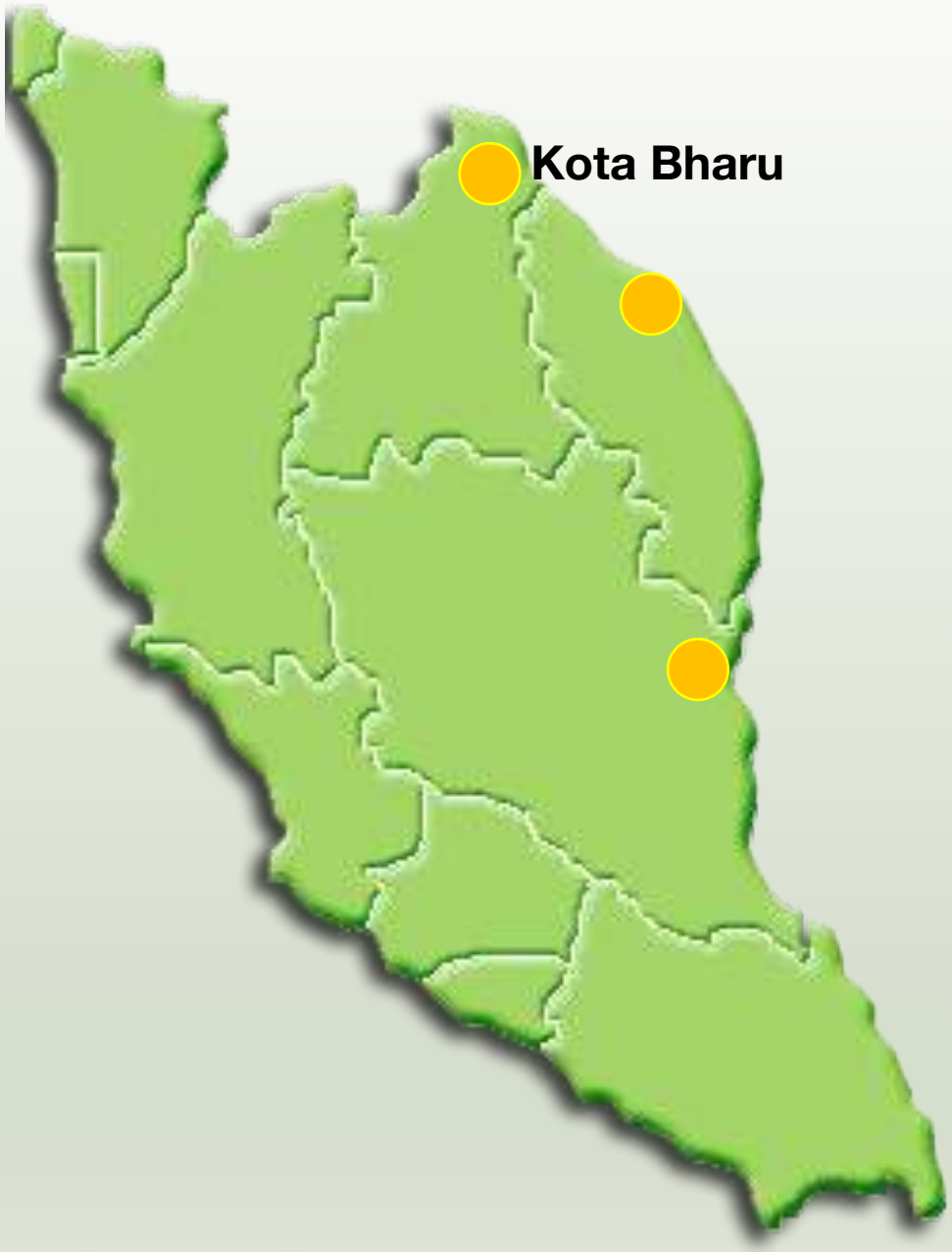
- Institute for Medical Research (IMR)
- Department of Chemistry Malaysia
- UMMC University Malaya
- MGL Universiti Putra Malaysia
- UMBI Universiti Kebangsaan Malaysia
- Hospital Kuala Lumpur

Private Laboratories

- Malaysian Genomic Research Centre
- DNA Lab
- GenomixLab
- Roche-Foundation Medicine Inc
- Gribbles Pathology
- Cancer Research Malaysia
- Prince Court Medical Centre
- Sengenics

- Advance Medical & Dental Institute (AMDI), USM
- Centre For Chemical Biology (CCB), USM
- Pantai Premier Pathology
- Gribbles Pathology

Penang



East Coast Peninsular Malaysia

- Human Genome Centre, USM
- INFORMM, USM
- Hematology Lab, USM
- Gribbles Pathology in Kota Bharu, Kuantan & Kuala Terengganu
- Pantai Premier Pathology in Kota Bharu, Kuantan & Kuala Terengganu


SOUTH CHINA SEA
BORNEO
Kota Kinabalu
MALAYSIA
Kotabalu
National Park
SABAH
BRUNEI
Damai Specialist Hospital
Sarawak General Hospital
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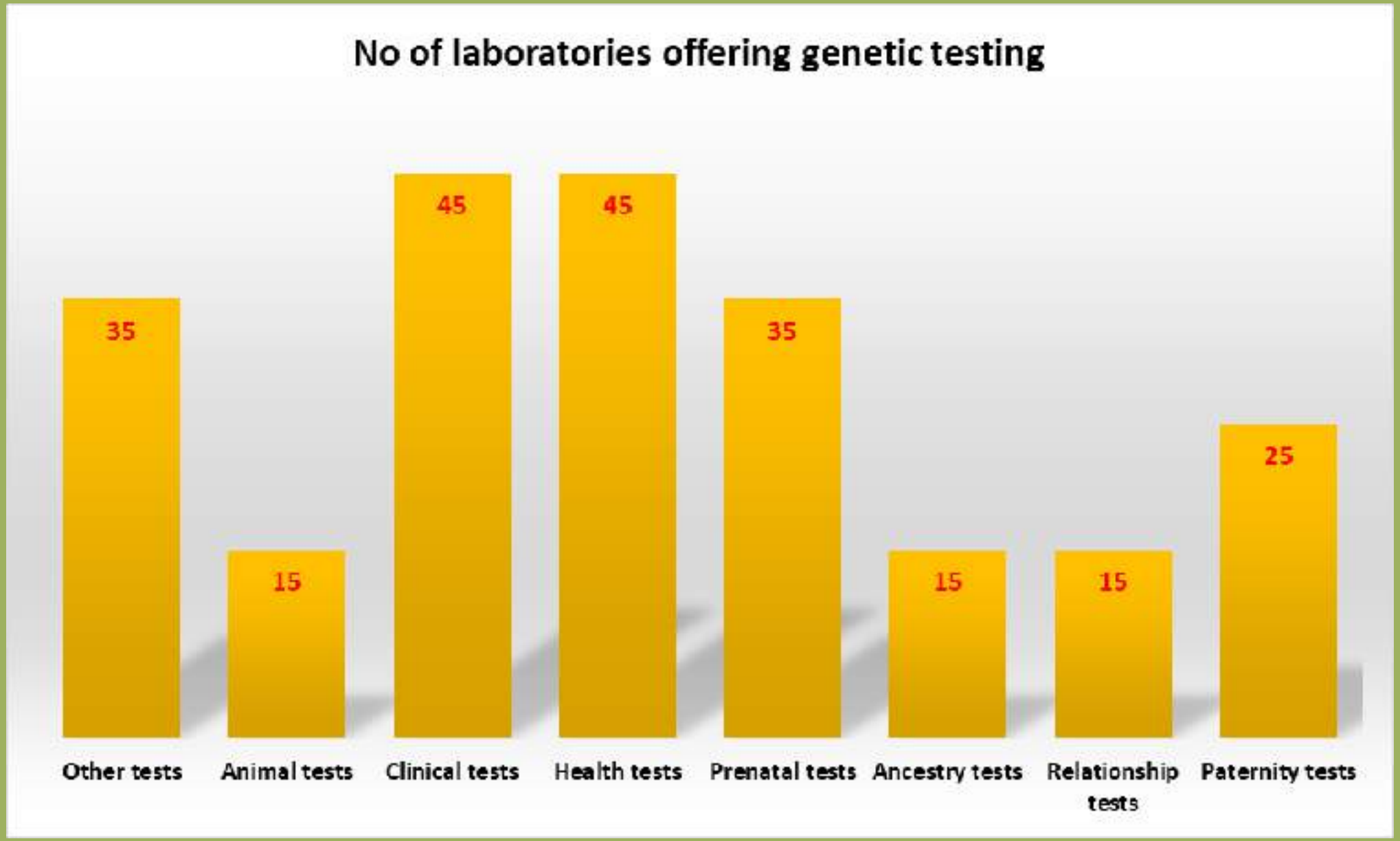
BRUNEI
DARUSSALAM
Limbang
Miri
Genung
Mulu National
Park
Niah Caves
National Park
SOUTH CHINA SEA
SULU SEA
Bintulu
Mukah
Kuching Specialist Hospital
Labuan
Sibu
Sarikei
Bako
National Park
Kuching
Bandar Sri Aman
Brunei
Sarawak
KALIMANTAN

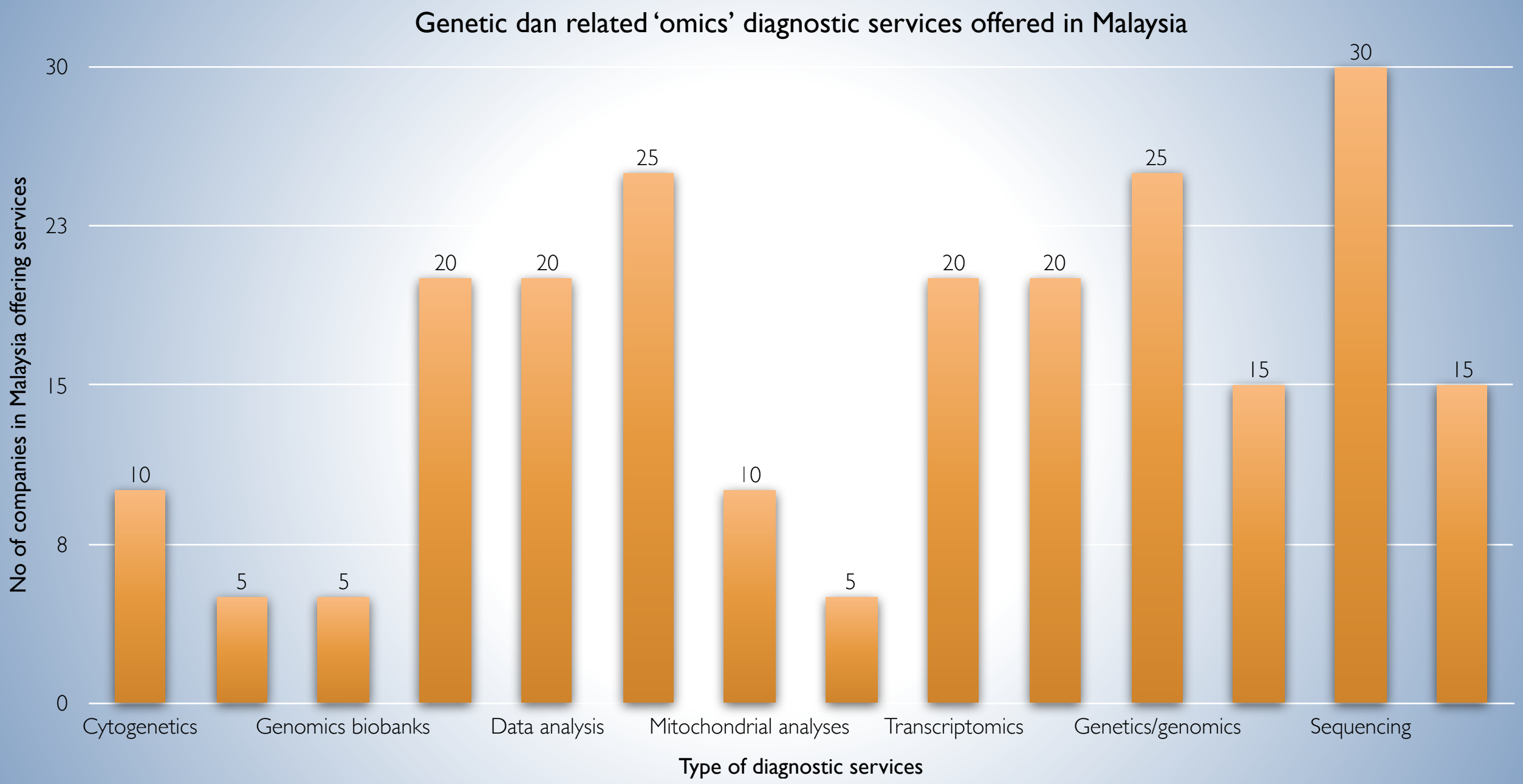
GENETIC TESTING SERVICES OFFERED IN MALAYSIA



Balasopoulou *et al* 2017

GENETIC TESTING IN MALAYSIA

- 40% Malaysian genetic testing lab offer lifestyle genomic test (fitness & wellness)
- 35% offer prenatal testing services
- 15% offer relationship/ancestry tests
- 15% offer pharmacogenomic tests
-



Balasopoulou et al 2017

Genomic biobanking

- Malaysia Genome Institute (bacteria, yeast, fungi)
- UMBI, Universiti Kebangsaan Malaysia (human for Malaysian Cohort)
- Malaysian Oral Cancer Database and Tissue Bank System (MOCDTBS), Malaysian Periodontal Database & Biobank System (MPDBS) (human)
- Malaysian Agriculture Research and Development Institute (Plant, bacteria, fungi)
- Renexus Group (Malaysian flora and fauna)

Pharmacogenetics/genomics

- Fisher Scientific
- Gribbles Pathology

Genomic analysis

- Malaysian Genome Resource Centre
- Malaysia Genome Institute

Bioinformatics analysis

- iPromise, UiTM
- Malaysia Genome Institute
- Genome Solutions Sdn Bhd
- Genomax technologies Malaysia
- Sengenics
- MGRC

Malaysian Periodontal Database and Biobank System (MPDBS) include University of Malaya; University Technology Mara; Universiti Sains Islam Malaysia; Ministry of Health, Malaysia

GENOM MALAYSIA
Malaysia Genome Institute

MALAYSIA GENOME INSTITUTE

Sequencing Services

- Illumina HiSeq 2000
- Illumina MiSeq 5 System
- Sanger DNA Sequencing

Read More

Genomic Biobank Services

- Long-term biospecimens storage for cells (bacteria, yeast, fungi), genetic vectors (DNA, RNA) and proteins
- Freezer rentals with biobank biospecimens
- Low temperature resistant barcode label printing

Read More

Genome Computing Centre Services

- Genome Assembly and Annotation
- Transcriptome and Differential Expression Analysis
- Phylogenetics
- Misc. Sequence Analyses
- Misc. Sequence Analyses

Read More

Proteomics Services

- Protein Identification and Quantification
- Molecular Weight Determination
- De Novo Peptide Sequencing

Metabolomics Services

- Qualitative LCMS Analysis
- Quantitative LCMS Analysis

Read More

Protein Expression and Purification Services

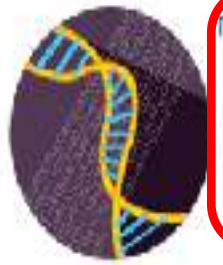
- Recombinant Protein Expression
- Protein Purification

Read More

Synthetic Biology and Cell Factory Services

- Sequence and construct optimisation
- Site-directed mutagenesis(SDM)
- Dna cloning
- Gene deletion/insertion(genome modification)

Read More



Bioinformatics Analysis Services

- Genome Assembly and Annotation
- Structural Modeling
- Transcriptome and Differential Expression Analysis
- Phylogenetics
- Misc. Sequence Analyses

Read More

Structural Biology and Biophysics Services

- Bruker Avance 700 MHz NMR
- Single X-ray Diffractor System
- DiaCore X 100 Plus
- JASCO J-815 Circular Dichroism Spectrometer (CD)
- PHOENIX Liquid Handling & Microscope System
- Nano Isothermal Titration Calorimetry (Nano- ITC)
- MicroCal VP-Differential Scanning Calorimetry (VP - DSC)
- DiaCore X 100 Plus
- Cary Eclipse Fluorescence Spectrometer
- Dynamic Light Scattering (DLS), Viscotek 802

Read More

DNA LAB (MOLECULAR DIAGNOSTICS) SDN BHD

NGS-based Screening

- Pre-natal testing
- EmbryoCheck - Pre-Implantation Genetic Screening (PGS)
- Cancer screening

PRODUCT CATEGORIES

- Chemicals & Reagents
- Chromatography Consumables
- Healthcare
  - → Histopathology
  - → Molecular Biology
    - Agena – Instruments
      - MassARRAY Systems
    - Agena – Panels
      - Blood Typing Panels
      - Cancer Panels
      - Custom Panels
      - Cystic Fibrosis
      - Pharmacogenetics
      - Sample Identification and Qualification Panels
    - Agena – Reagents
      - iPLEX® Chemistry
      - UltraSEEK™ Chemistry

Pharmacogenetics

Agena Bioscience offers an array of pharmacogenetic (PGx) panels for use with the MassARRAY® System, enabling you to cost-effectively detect germline variations that cause differences in drug distribution, efficacy, metabolism, and toxicity. Our PGx panels can be used for routine pharmacogenetic testing to determine drug metabolizer status, stratify clinical trial participants into metabolizer types, or validate PGx markers discovered through genome wide association studies in hundreds of additional samples.

Reliable, Precise Detection

- Detect SNPs, indel variations, and CNVs in a single assay.
- Haplotype reports are rapidly generated from genotyping data with automated software tools.
- 24-, 96- and 384-well formats offer the flexibility to generate results from 10s to 1000s of samples a day.

iPLEX PGx Pro Panel

Covers 99% of the most relevant pharmacogenetic markers considered to be broadly applicable to clinical trials. Interrogates 191 SNPs in 36 key genes, including *CYP2C9*, *CYP2C19*, *CYP2D6*, and *UGT1A1*.

PGx 68 Panel

Interrogates 63 SNPs in 16 genes and 5 CNV assays, covering most of the important haplotypes of each gene.

CYP2C9 / VKORC1 Panel

Obtain biologically-relevant data for most of the known haplotypes of each gene. Interrogates 38 SNPs in *CYP2C9* and 11 SNPs in *VKORC1*.

CYP2C19 Panel

Investigate and confirm pharmacogenetic biomarkers in *CYP2C19*. The panel contains assays for 31 SNPs, covering most of the known *CYP2C19* haplotypes.

CYP2D6 Panel

The *CYP2D6* Panel is a set of 30 SNP and 5 CNV assays, covering most of the known *CYP2D6* haplotypes.

FISHER SCIENTIFIC

fisher scientific
part of Thermo Fisher Scientific

MALAYSIAN GENOMIC RESOURCE CENTRE

NGS-based applications that includes plant, animal, microbial & human genomes.

- Whole Genome Sequencing (WGS)
- Transcriptome
- Metagenomics & Metatranscriptomics
- Genetic Screening

ASIA-GENOMICS

Services offered

1. Test panels
   - Reproductive
     - Carrier Screening
     - Non-invasive Prenatal Test
     - Newborn Screening
   - Hereditary Cancers
   - Somatic Cancers
2. Genetic Counseling Support Services

asiagenomics

DELIVERING NGS TO MALAYSIAN DIAGNOSTIC SETTING

- Expansion of knowledge through research work & its application to clinical practice in Malaysia reflect a strong interest in exploration of genetic diversity & the elucidation of genetic basis of diseases.
- Since 2015, Universiti Malaya & Golden Helix Foundation collaborate to establish public health policies in areas of pharmacogenomics & precision medicine.
- Increased awareness among Malaysian on the importance of precision genomic & increasing number of genetic analysis services offered by public & private institutions
  - Pave ways to expansion of NGS based analysis implementation in diagnostic setting.

MALAYSIAN NODE OF HUMAN VARIOME PROJECT (MyHVP)

2010
Malaysian Node of Human Variome Project

- Lau… UPM, Serd…
- Hea… M
- 69 … rious inst… ding USM, MM… ver… Malaysia, Medical Genetics Society of Malaysia, Genetics Society of Malaysia, Sengenics, Synamatix, Malaysian Society of Bioinformatics & Computational Biology, & Jabatan Kimia Malaysia.

MyHVPDb
Launched
2010

- Genetic variants for genetic diseases prevalent in Malaysia
- Malay whole genome SNPs data

EduVariome
Launched
2014

Education on inherited genetic diseases focus on thalassemia

Target audience – high schoolers and university students

GG2020 Challenge
Launched
2015

Focus on haemoglobinopathies in low - middle income countries (LMIC)

S… …g ceremony of MyHVP and SNP Malay

MyHVP

GENOMICS FOR ALL

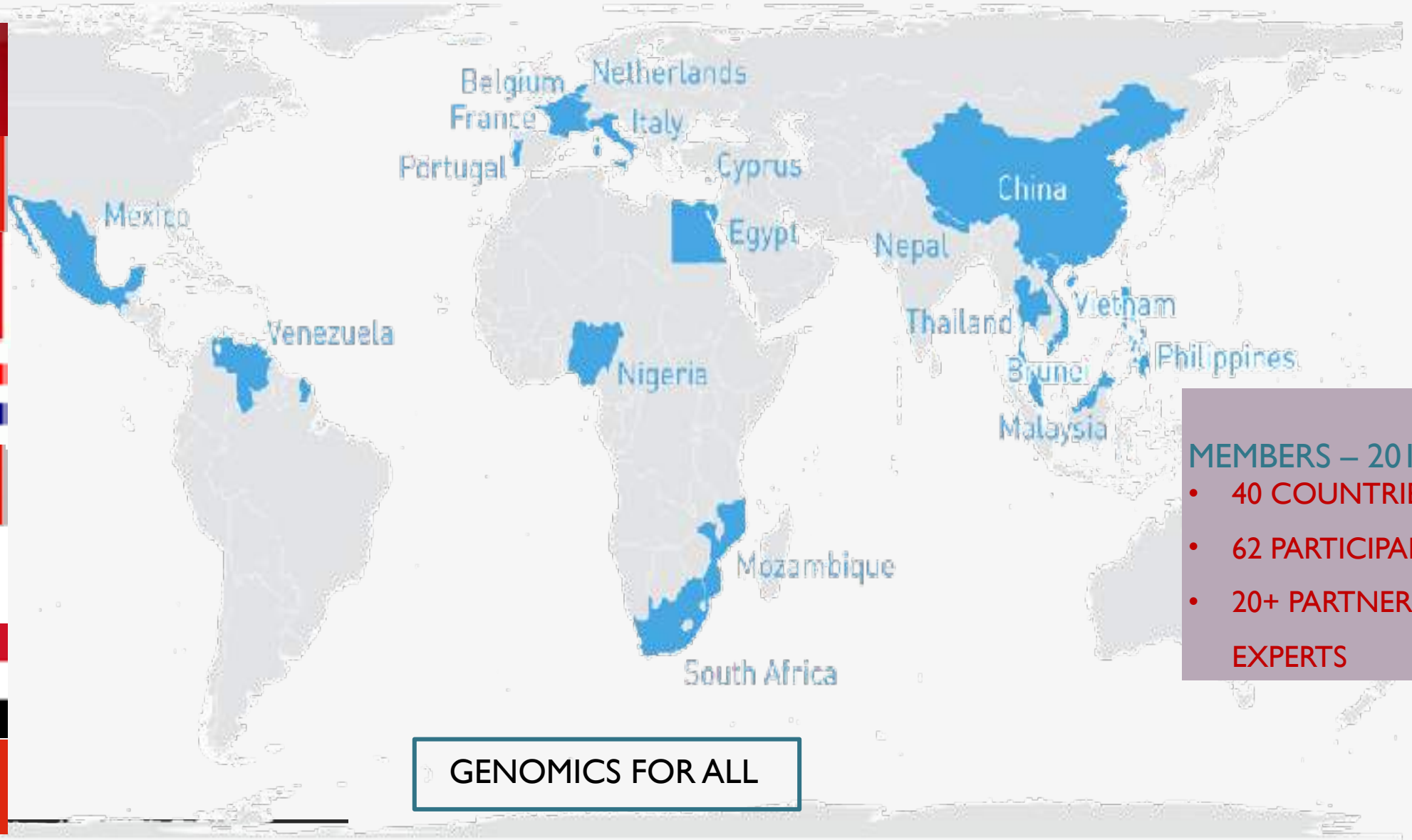
GLOBAL GLOBIN 2020 CHALLENGE 2015

- To apply recent developments in human genomics involving systematic collection & sharing of Variation data to fighting haemoglobinopathies in low- and middle-income countries (LMICs)
- Designed to build capacity for genomic diagnosis and clinical services and research

GG2020 linked to ITHANET through a shared ITHANET-GG2020 Expert Panel application for haemoglobinopathy-related variant classification under Clinical Genome (ClinGen) Resource

www.thehumanvariomeproject.org/GG2020

GG2020
PARTICIPATING COUNTRIES



MEMBERS – 2016

- 40 COUNTRIES
- 62 PARTICIPANTS
- 20+ PARTNERS, EXPERTS

GENOMICS FOR ALL

BUILDING BLOCKS

Guidelines for diagnostic NGS

By EuroGentest and the European Society of Human Genetics, 2015

1. NGS should not be transferred to clinical practice without an acceptable validation of the tests according to the emerging guidelines.
2. a
3. be
4. When a laboratory is considering introducing NGS in diagnostics, it first has to consider the diagnostic yield.
5. pe
6. be
7. between laboratories.

NGS **should not be transferred to clinical practice without an acceptable validation** of the tests according to the emerging guidelines.

For diagnostic purpose, only **genes with a known** (ie, published & confirmed) **relationship between the aberrant genotype & the pathology** should be included in the analysis.

Matthijs *et al* 2016. European Journal of Human Genetics, 24, 2–5; doi:10.1038/ejhg.2015.226

The laboratory has to provide for each NGS test the following: the **diseases it targets**, the **name of the genes tested**, their **reportable range**, the **analytical sensitivity & specificity**, and, if possible, the **diseases** not relevant to the clinical phenotype that **could be caused by mutations in the tested genes**.

Laboratories should **provide information** on the chance of **unsolicited findings**.

The diagnostic laboratory has to implement a **structured database** for relevant quality measures for (i) the **platform**, (ii) all **assays**, and (iii) all **samples processed**.

17. Accuracy and precision should be part of the general platform validation, and the work does not have to be repeated for individual methods or tests.
18. The bioinformatics pipeline must be tailored for the technical platform used.
19. A
20. T
21. The diagnostic laboratory has to implement/use a structured database for all relevant variants with current annotations.
22. T
23. T
during the test development and should be available to the clinician (either in the report or communicated digitally).
24. The requirements for 'reportable range' depend on the aim of the assay.
25. V

Accuracy and precision should be part of the general platform validation, and the work does not have to be repeated for individual methods or tests.

The bioinformatics pipeline must be tailored for the technical platform used.

The diagnostic laboratory has to validate all parts of the bioinformatic pipeline with a standard & structured database for all relevant variants with current annotations.

Data on unclassified variants (UVs) have to be collected, with the aim to eventually classify these variants definitively.

Laboratories should have a clearly defined protocol for addressing unsolicited and secondary findings prior to launching the test

The laboratory is not expected to re-analyze old data systematically and report novel findings, not even when the core disease gene panel changes.

To be able to manage disease variants, the laboratory has to set up a local variant database for the different diseases for which testing is offered on a clinical basis.

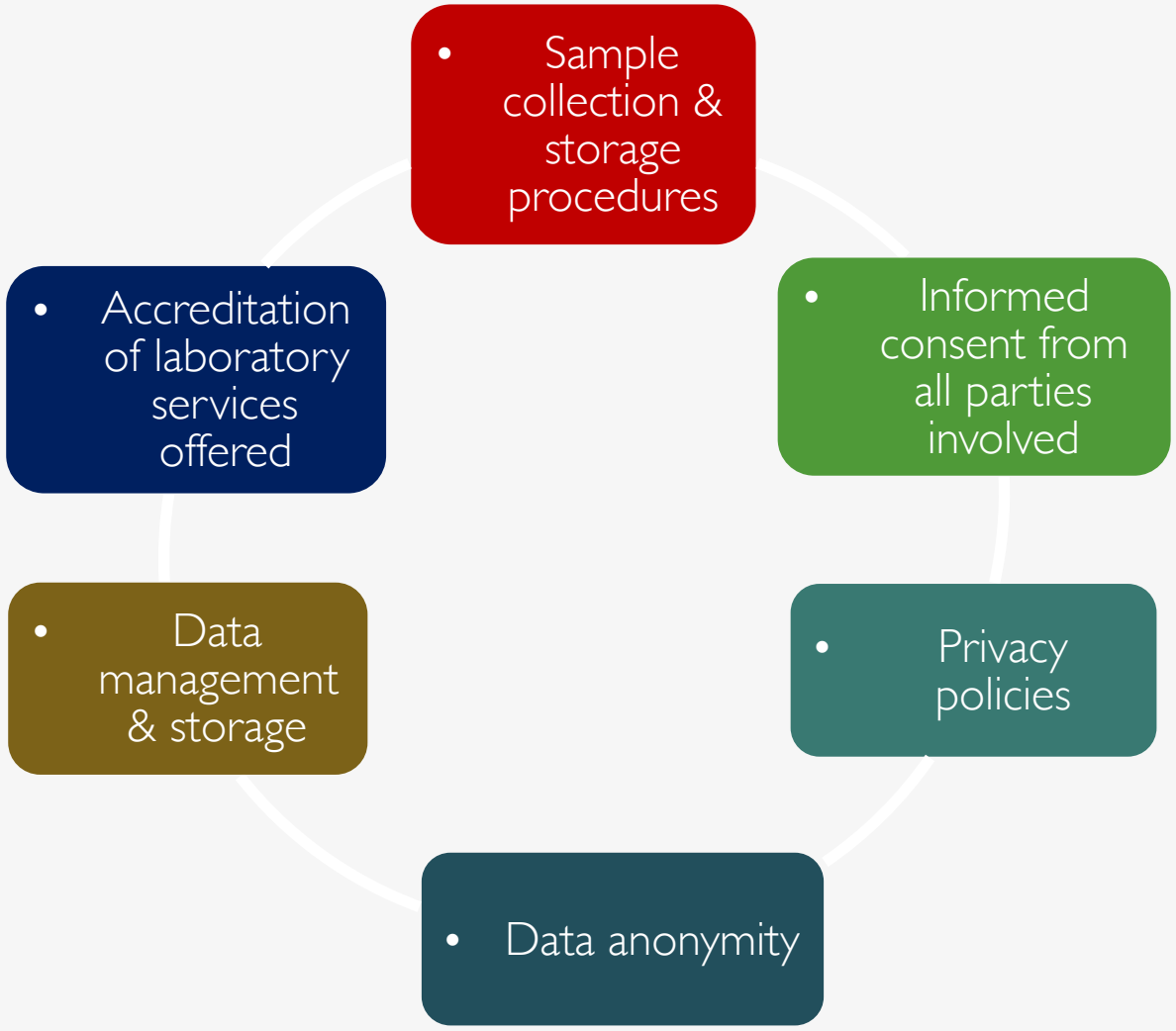
Diagnostic tests that have as their primary aim to search for a diagnosis in a single patient should be performed in an accredited laboratory.

Research results have to be confirmed in an accredited laboratory before being transferred to the patient

All **reported variants should be shared** by submission to federated, regional, national, and/or international databases

Requirements for clinical diagnostic application

Service operation procedure must include



Issues to address

Cost

- Estimated cost of establishing a facility ranges USD100 K - USD700 K.
- The expense far exceeds available funds for scientists in most developing countries.

Ethical concerns

- Most genetic testing laboratories provide extremely limited information about DNA isolation, informed consents, sample storage & privacy policy issues.

Data analyses

- Ability to analyze our genome rapidly led to a burst of information to be interpreted.
- However lack of bioinformatician to decipher the abundance of results

Refs: El-Metwally et al. 2014, Balasoupoulou et al. 2017, Lee & Thong 2013, Ngim et al. 2013

Awareness

- Lack of awareness on the importance of genetic testing among Malaysian population.
  - Screening for monogenic diseases such as thalassemia
- Low awareness and knowledge among medical practitioner and public
  - Importance of pharmacogenetic testing in translating patient's genetic profile for optimum drug therapy for a more personalised treatment. Eg: Cancer treatment

Genetic counselling

- Low number of genetic counsellors & clinical geneticist with knowledge & expertise to properly inform patients about their clinical phenotype, prognosis of the disease, risks of recurrence & disease prevention and treatment.

High cost

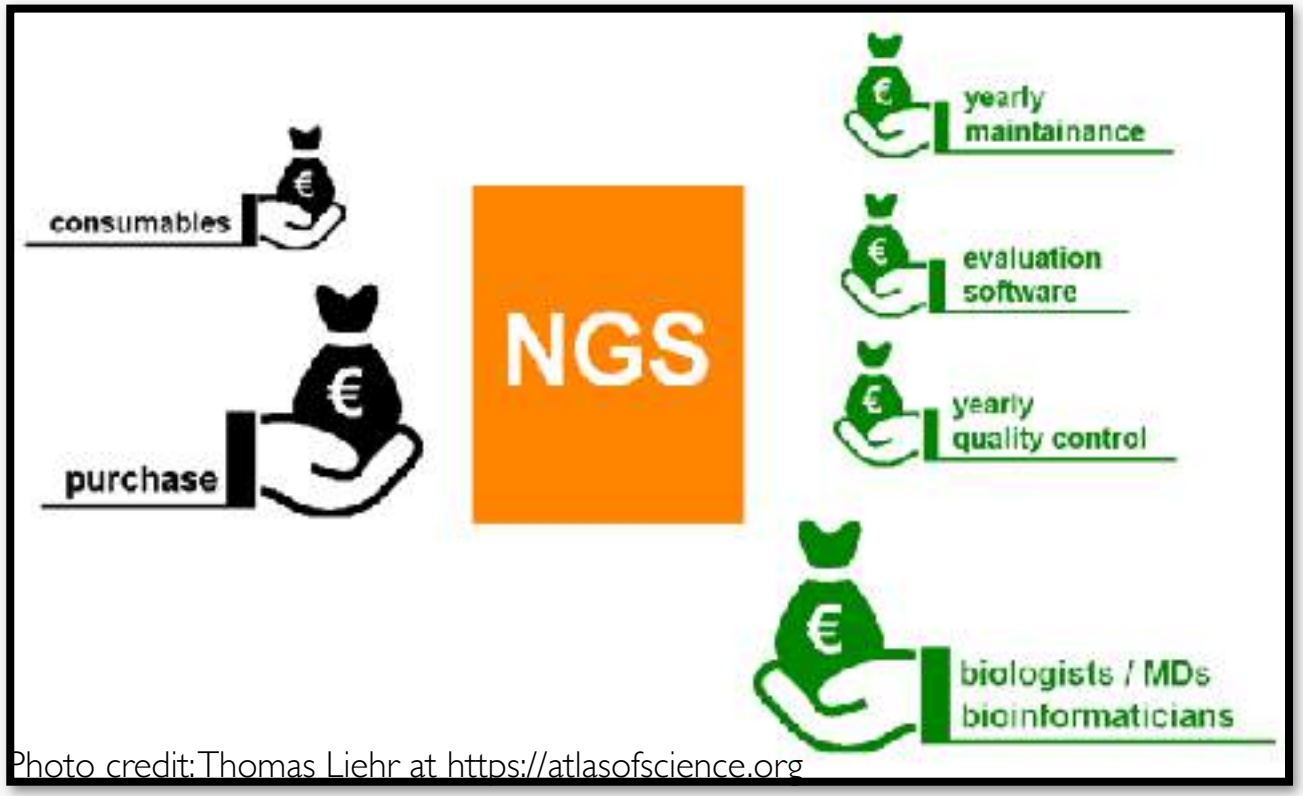


Photo credit: Thomas Liehr at https://atlasofscience.org

Costs in connection with NGS – those which are normally considered and discussed (in black), those which are normally not considered (in green).

- In spite of the remarkable increase in speed & decrease in costs, establishing a genome sequencing facility with NGS technology remains challenging esp to the under-developed world.
  - High cost of establishing & maintaining a sequencing facility.
- By realizing the importance of genomic research & its applications on health, drugs & food security, governmental policies should prioritize research funding for genomics research & clinical application.

Ethics in NGS

- The genome sequencing research & clinical applications can involve sensitive information
  - ie: personal data (name, gender, date of birth, race), medical history & family history with diseases.
  - Such information should be handled carefully with restricted regulations to protect the privacy and maintain the anonymity of the source of the sample.
- Informed consent:
  - Individuals, whether they are well or ill or participating in a research study, need to be informed during the consent process about the exact specifics of the proposed analysis.

- **American College of Medical Genetics and Genomics (ACMG) recommended**
  - Incidental findings (Ifs) may be reported to patients (or parents) whether the genomic analysis has been undertaken in a diagnostic or a research context.

  - Include a list of 56 genes, in which they recommend the active return of results when a likely disease-causing mutation is identified in adult or paediatric (but not foetal) samples.
    - In which mutation causes a serious health problem for which early diagnosis and intervention can make a major difference to outcomes.

- **Universiti Sains Malaysia Human Research Ethics Committee proposed that for Whole-Genome studies:**
    - Researchers are required to determine if study results (incidental or otherwise) meet the criteria for offering the information to individual participants.

    - The process of identifying and disclosing research results should involve professionals with the appropriate expertise required to provide the participant with sufficient interpretive information.
      - The results offered should be scientifically valid, confirmed, & should have significant implications for the subject's health and well-being.

Data analyses

Clinical Interpretation

- A major challenge of delivering genomic tests along with coherent, consistent & reliable interpretation of sequencing variants esp as it pertains to patient care.
  - Typical exome sample will have 10,000 - 20,000 variants
  - Whole-genome sample generally have >3 million.
- Gaps between bioinformaticians & clinicians must be overcame to convert the raw data generated to comprehensible clinical diagnosis.
- To make things more manageable, variants are filtered based on their likelihood to cause disease.
- American College of Medical Genetics & Genomics, Association for Molecular Pathology & College of American Pathologists created a system for classifying variants:
  - Pathogenic, likely pathogenic, uncertain significance, likely benign, & benign.

Photo credit: https://www.aacc.org

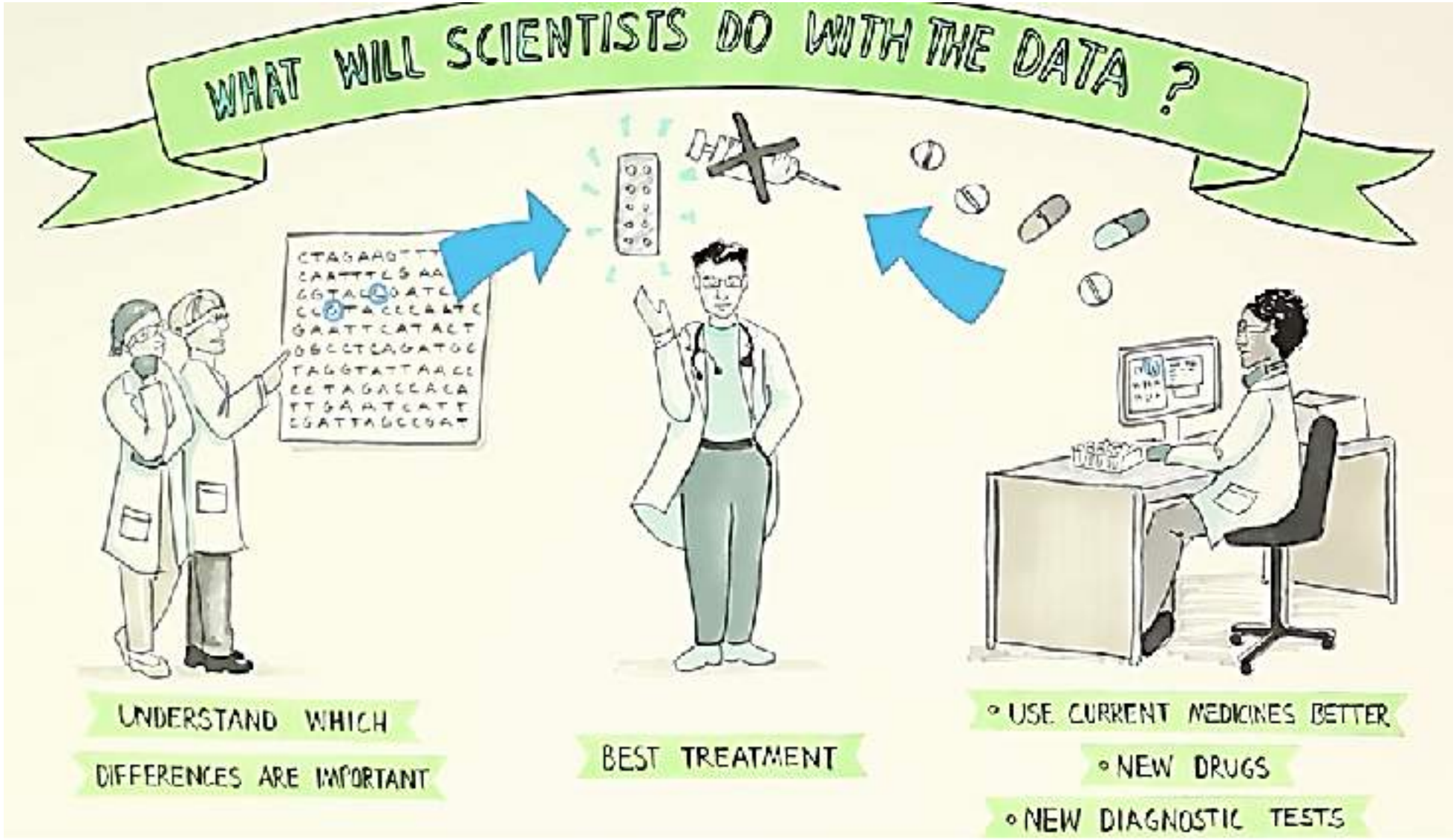


Photo credit: Genomics England

Ethical data management

- NGS (whole genome & exomes) generates additional information, including unsought & unwanted information.
  - Must be deliberately managed—interpreted, disclosed & then either stored or destroyed.
- New SNPs from NGS whole genome & exomes results must be assessed for their validity & utility before disclosure to avoid "over-reporting" by clinicians based solely on basic discovery of research
  - Need to rethink the boundaries between clinical & research practice

Awareness

- Insufficient genomics education & lack of genomics awareness among general public & healthcare professionals hinders smooth incorporation of genomic medicine into clinical practice.
  - Vast majority of health-care professionals feel insufficiently trained in genomics to be able to engage with delivery of genome-based services
  - Patients & public tend to have low genomic literacy - impairs capacity to successfully integrate genome based information into personal decision-making.

- Genomics needs to be more uniformly & extensively taught.
  - Need for in-depth genomics education highlighted
  - Incorporation of pharmacogenomics & genomic medicine in undergraduate / graduate training, or in form of continuous medical education seminars.

Ref: Mitropoulos et al. 2015

MASTER OF PATHOLOGY (MEDICAL GENETICS)

MPATH MED GENETICS

Human Genome Center, School of Medical Sciences
University Sains Malaysia

- **Name of the Programme –**

  Master of Pathology (Medical Genetics)
- **Name of Degree -**

  M Path (Medical Genetics)
- **Level of Programme –**

  4-years mixed mode Masters training programme
- **Offering institutions -**

  Human Genome Center (USM), School of Medical Sciences in collaboration with:

Inside USM Health Campus	Outside USM Health Campus
Pediatric ward/clinic	Cytogenetic Lab, HKL
Hematology Lab	Biochemistry Unit, IMR
Oncology ward/clinic	DNA Lab, UKM
Chemical Pathology Lab	Cytogenetic Lab, IPPT

Genetic counselling

- Still no formal recognition of the role of genetic counsellors in Malaysia & no legal requirements for the provision of genetic counselling services.
- Some genetic counsellors, often lack knowledge, expertise, & skills to properly inform patients & their families, about the clinical phenotype & prognosis of a disease, risks of disease recurrence, and options for disease prevention & treatment arising from the NGS analysis.
- To date, **only one formal Masters programme for genetic counselling offered by National University of Malaysia (UKM).**
- Medical genetics professionals, representatives from the Ministry of Health, universities & public service commission need to create more programmes with appropriate career pathways for qualified genetic counsellors.

Summary

- The implementation of NGS **as a routine diagnostic test** in Malaysia is challenging as there is a lack of government funding, equipment cost, lack of bioinformaticians & trained personnel to administer the system, lack of professional & public awareness, & a very low number of genetic counsellors.
- However, in the next decade the application of NGS is expected to progressively replace the conventional Sanger sequencing in diagnostic setting. A number of diagnostic centres, public and private, have started offering services but the demand for such services within the country is small.
- Identification of the current gaps and possible corrective actions to improve the quality of genomics & predictive analytics utilising NGS in Malaysian clinical diagnostic setting is important to enable the setting up of a successful & accredited clinical diagnostic laboratories.

ACKNOWLEDGEMENT

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"We are born with the genes, and genes don't lie. It's what you do upon knowing that counts. It may just save your life or prolong it even…"